EXHIBIT A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Sergei A. Svarovsky et al.**	Confirmation No.: **2177**
Application No.: **10/594,075**	Group Art Unit: **1641**
Filing Date: **August 14, 2007**	Examiner: **Shafiqul HAQ**

For: **Carbohydrate-Encapsulated Quantum Dots for Biological Imaging**

DECLARATION OF JOSEPH J. BARCHI, JR., PH.D. UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, **Joseph J. Barchi, Jr., Ph.D.**, hereby declare that:

1. I am a Senior Scientist and the Head of theStructural Glycoconjugate Chemistry and NMR Group of Chemical Biology Laboratory of the Center for Cancer Research for the National Cancer Institute in Frederick, Maryland. A copy of my curriculum vitae is attached hereto as **Exhibit B**.
2. I am a named co-inventor on United States Patent Application 10/594,075, filed on August 14, 2007, with the United States Patent and Trademark Office (the "subject application"). I am familiar with the subject application.
3. I understand that the pending claims of the subject application have been finally rejected as allegedly unpatentable over the following references:
    a. Zheng, M. *et al.*, "Ethylene Glycol Monolayer Protected Nanoparticles for Eliminating Nonspecific Binding with Biological Molecules", **2003,** *J. Am. Chem. Soc.* 125, pp. 7790-7791. ("Zheng")
    b. Lin, C-C. *et al.*, "Selective Binding of Mannose-Encapsulated Gold Nanoparticles to Type 1 Pili in *Escherichia coli*", **2002,** *J. Am. Chem. Soc.* 124, pp. 3508-3509. ("Lin")

c. U.S. Patent No. 6,306,610 B1 issued to Bawendi et al. on October 23, 2001. ("Bawendi")
d. Barrientos, A. G., *et al.*, "Gold Glyconanoparticles: Synthetic Polyvalent Ligands Mimicking Glycocalyx-Like Surfaces as Tools for Glycobiological Studies", **2003,** *Chem. Eur. J.,* 9, pp. 1909-1921. ("Barrientos")
e. Bruchez, M. Jr., *et al.*, "Semiconductor Nanocrystals as Fluorescent Biological Labels", **1998,** *Science,* 281, pp. 2013-2016. ("Bruchez")

4. It has been explained to me that claims 95, 98, 150 and 155 of the subject application have been rejected as allegedly obvious in view of the Zheng, Lin and Bawendi references.
5. I is my view that one of ordinary skill in the art would not understand how the Lin and Bawendi references would provide any motivation to modify the disclosure of the Zheng reference to arrive at the invention claimed in the subject application.
6. It is my further view that one of ordinary skill in the art would understand the Zheng reference to be directed to solving problems associated with non-specific binding of metallic nanomaterials with biological molecules via electrostatic interactions, which is quite different than the invention claimed in the subject application.
7. My understanding of the Zheng reference is informed by my experience in the field of glycoconjugate chemistry and nanoparticles.
8. The Zheng reference describes generally that it is recognized that the surfaces of many metallic nanoparticles, such as Au, Ag, Pt and Cu are charged, which cause nonspecific binding with biological molecules via electrostatic interactions (Zheng, p. 7790, left col., first par., ll. 7-10).

9. As explained further in this paragraph of Zheng, nonspecific binding between nanoparticles and biomolecules is a fundamental issue that is not well addressed in the published literature.

10. Zheng solves the problem of the electrostatic-driven non-specific binding between metallic gold nanoparticles and biological molecules by bonding a uniform monolayer of di-, tri-, and tetra(ethylene glycol) to the surfaces of the gold nanoparticles.

11. It is known that noble metal nanoparticles, like gold and silver, are conductors and so they do not have a band gap. For this reason metallic nanoparticles do not typically luminesce. Instead, these materials are characterized by intense, size-dependent surface plasmon absorption in the visible or near-ultraviolet region when the particle size is decreased below the de Broglie wavelength of 20 nm. When electrons are promoted into the conduction band, they become trapped and exhibit a characteristic oscillation known as the surface plasmon band. If the wavelength of incident light corresponds to that of the conduction band electrons, enhanced oscillation of the electron cloud results. This is referred to as the localized surface plasmon resonance (LSPR). The result is a strong absorbance at an energy that is unique for sufficiently small (~5-20 nm) noble metal nanoparticles.

12. It is known that the LSPR is sensitive to changes in refractive index that can be incurred by changes in particle size and/or surface functionalization of metallic nanoparticles.

13. Accordingly, surface functionalization methods must be very specifically tailored to the type and size of noble metal nanoparticles to ensure that LSPR occurs.

14. As a result, the surface functionalization methods that may very well be useful for allowing noble metal nanoparticles to exhibit LSPR would not motivate one of ordinary skill in the art to use the same functionalization startegies on luminescing nanoparticles that exhibit a band gap, such as those claimed in the subject application.

15. Because the Zheng reference discloses only the problems associated with the charged surfaces of metallic nanoparticles, one of skill in the art would not be motivated to look towards the Zheng reference as a starting point for making quantum dots capable of luminescing and comprising a nanocrystalline core exhibiting quantum confinement and having a band gap as claimed in the subject application.

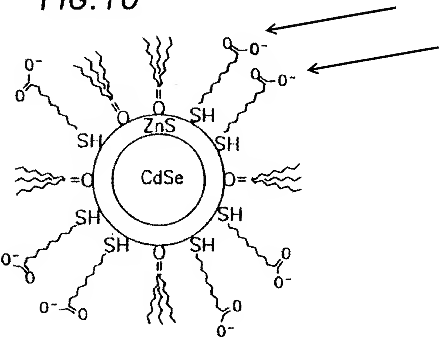
16. The Lin reference is also directed to metallic gold nanoparticles that are quite unlike the nanoparticles claimed in the subject application. The examiner had indicated (final rejection page 4, second full paragraph), that Lin teaches that besides gold nanoparticles, semiconductor nanoparticle bioconjugates as selective fluorescent biological labels have shown great potential in biological studies and medical applications (Lin, ll. 1-13, 1st col, p. 3508). This may be so, generally speaking, but Lin still does not teach any chemical methods or compositions specifically in connection with semiconductor quantum dots having a band gap as claimed in the subject application.

17. In fact, the Lin reference is primarily directed to gold nanoparticles, as indicated by the title and its recitation of the technical advantages of applying gold nanoparticles in biological systems all throughout the second full paragraph of the Lin reference.

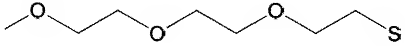
18. As well, the entire technical description and analyses in Lin is directed to gold nanoparticles. None of the described chemistry in Lin is directed to the semiconductor quantum dots having a band gap as claimed in the subject application.

19. The Bawendi patent discloses functionalizing semiconducting nanoparticles with thiols. However, the particular thiols of Bawendi in Figure 10 (indicated below by arrows) the examiner refers to in the final rejection in the third full paragraph of page 4 are actually charged thiols ending in charged carboxylic acid groups. These are quite different from the mercapto triethylene glycol group that does not have an associated charge in solution.

FIG. 10



20. Indeed, claim 155 is directed to luminescence promoters comprising a plurality of mercapto triethylene glycol groups of the formula



,

which formula has a methoxy group on the left end; this is completely different than the charged carboxylic acid groups shown in Bawendi Figure 10.

21. It has also been explained to me that claims 95 and 98 of the subject application have been rejected as allegedly obvious in view of the Barrientos reference in view of the Lin, Bruchez, Bawendi and Zheng references.

22. I is my view that one of ordinary skill in the art would not understand how the Lin, Bruchez, Bawendi and Zheng references would provide any motivation to modify the disclosure of the Barrientos reference to arrive at the invention claimed in the subject application.

23. It is my further view that one of ordinary skill in the art would understand the Barrientos reference to be directed to solving problems associated with attaching sugar molecules to gold particles.

24. My understanding of the Barrientos reference is informed by my experience in the field of glycoconjugate chemistry and nanoparticles.

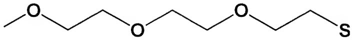
25. The Barrientos reference describes methods for tailoring sugar-functionalized gold nanoclusters that have 3D polyvalent carbohydrate display and globular shapes. (Barrientos, Absract).

26. None of the ligands disclosed in the Barrientos reference include mercapto triethylene glycol groups as claimed in the subject application.

27. As well, one or ordinary skill in the art would not look to any one or combination of the Lin, Bruchez, Bawendi and Zheng references to motivate one of ordinary skill in the art to prepare quantum dots that include a luminescence promoter comprising a mercapto triethylene glycol group that does not have an associated charge in solution.

28. Specifically, one of ordinary skill in the art would not be motivated from these references to use a mercapto triethylene glycol group derived from mTEG (methoxy-TriEthylene Glycol) or derived from mTEG-SH (methoxy-TriEthyleneGlycol thiol).

29. As I stated above, an example of such a luminescence promoter can be represented by the following formula:



In this formula, the sulfur at the right end of the luminescence promoter as shown above is bonded to the nanocrystalline core having a band gap. The methoxy group on the left end of the luminescence promoter as shown above helps to prevent the generation of an associated charge in solution, as described in the present application in Example 26, paragraph [0181]. Indeed, we found this type of luminescence promoter to provide superior results (i.e., bright and stable quantum dots) compared to quantum dots not having such a luminescence promoter.

30. I declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further, that these

statements were made with the knowledge that willful false statements and the like are punishable by fine or by imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application, any patent issuing thereupon, or any patent to which this verified statement is directed.

Date: January 9, 2012

Signature: ______________________________
Joseph J. Barchi, Jr., Ph.D.

Attachments: **Exhibit B (curriculum vitae)**